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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/801,221	03/07/2001	Paul Sanberg	C14-135	5403

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EXAMINER	
FALK, ANNE MARIE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 01/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/801,221	SANBERG ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-20,43-61 and 70-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-20,43-61 and 70-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendments filed May 5, 2003 and June 20, 2003 have been entered. Claims 4-20 and 43-61 have been amended. Claims 1-3, 21-42, and 62-69 have been cancelled. Claims 70-86 have been newly added.

Accordingly, Claims 4-20, 43-61, and 70-86 are pending in the instant application.

The response filed October 14, 2003 has been entered. Applicants election with traverse of β-tubulin folding cofactor D as the gene associated with neurogenesis, is acknowledged. The traversal is on the grounds that the Examiner has not provided evidence that a search of all the neurogenesis associated genes listed would be seriously burdensome and that the MPEP states that "if the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the Examiner must examine all the members of the Markush group in the claims on the merits, even though they are directed to independent and distinct inventions." However, in the instant case the various genes listed in the claim are not properly members of a Markush group because they do not share a common structural feature. The various genes encode a great variety of structurally and functionally distinct proteins. The various genes would not be considered obvious variants. Given the substantial variation of the 30 neurogenesis-associated genes recited in the claims, a search and examination of all 30 genes would constitute a serious burden on the Office.

The requirement is still deemed proper and is therefore made FINAL.

The following rejections are reiterated or newly applied and constitute the complete set of rejections being applied to the instant application. Rejections and objections not reiterated from the previous office action are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-20 and 43-61 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced on pages 2-5 of the Office Action of Paper No. 4 (mailed 10/4/01), on pages 2-6 of the Office Action of Paper No. 9 (mailed 5/31/02), and for further reasons as discussed herein, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

At page 15 of the response, Applicants argue that pages 58-65 of the specification describe working examples that result in a therapeutic benefit. However, while the specification discloses the use of human cord blood fractions that have been used either directly upon thawing (cord blood mononuclear cells) or treated in culture for a week with various trophic factors (BDNF, NGF, EGF+bFGF) prior to transplantation, the claims cover the preparation of a great variety of cell compositions, including terminally-differentiated cells, which the specification does not teach how to use. The human cord blood fractions used directly upon thawing are not the cells produced by the claimed methods, but rather appear to be the starting material for use in the claimed method. With regard to the cells that were cultured with various trophic factors, the specification does not disclose the phenotype of these cells and the claims require the production of "neural cells."

Given the lack of applicable working examples, the limited guidance provided in the specification, the broad scope of the claims with regard to the wide variety of cell types and cell compositions that could be produced using the claimed methods, and the unpredictability for using the cell compositions produced to achieve a therapeutic effect upon transplantation as asserted in the

specification, undue experimentation would have been required for one skilled in the art to make and use the claimed cell compositions.

Thus, the rejection under 35 U.S.C. 112, first paragraph, is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-20, 43-61, and 72-86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4-20, 43-61, and 72-86 are indefinite in their recitation of "neural cells" because, as evidenced by the claim language of newly added Claim 75, Applicants apparently consider hematopoietic stem cells to constitute "neural cells." This interpretation is not conventional in the art and the specification does not provide a clear definition for the term "neural cells." Thus, the metes and bounds of the claims are not clearly set forth.

Claims 72-81 are indefinite in their recitation of "increase" and "decrease" because it is unclear what would be considered the reference state for said "increase" or said "decrease". The claims are directed to an isolated neural cell and said cell can clearly be viewed in a static state (i.e., not undergoing neurogenesis), even in the presence of a differentiation agent. In the absence of recitation of some reference state or process for comparison said "increase" and said "decrease" are indefinite.

Claim 76 is indefinite in its recitation of "[t]he isolated neural of claim 72" because one or more words appear to be missing.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 72-86 are rejected under 35 U.S.C. 102(a) as being anticipated by Kopen et al. (1999).

Claims 72-80 are directed to isolated neural cells obtainable from umbilical cord blood, wherein said neural cells exhibit both an increase in expression of genes associated with neurogenesis and a decrease in expression of genes associated with hematopoiesis when said neural cells are in the presence of an effective amount of a differentiation agent.

Claim 81 is directed to an isolated human multipotent neural progenitor cell obtainable from umbilical cord blood, wherein said neural progenitor cell exhibits both an increase in the expression of genes associated with neurogenesis and a decrease in expression of genes associated with hematopoiesis when said neural progenitor cell is in the presence of an effective amount of a differentiation agent.

Claims 82-86 are product-by-process claims. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. The patentability of a product does not depend on its method of production. See MPEP 2113. Thus, the claims read on neural cells disclosed in the prior art, as discussed below. There are no structural limitations to distinguish the claimed cells from any other neural cell.

Kopen et al. (1999) disclose that marrow stromal cells (MSCs, also mesenchymal stem cells) injected into the lateral ventricle of neonatal mice differentiated into astrocytes and neurons. Since mesenchymal stem cells are also present in umbilical cord blood the cells disclosed by Kopen et al. meet all the claim limitations.

Thus, the claimed compositions are disclosed in the prior art.

Claims 72-74 and 76-86 are rejected under 35 U.S.C. 102(b) as being anticipated by Dunbar et al. (1994).

In view of the claim language set forth in newly added Claim 75 reciting "wherein said neural cell is not a hematopoietic stem cell," it is evident that Applicants consider hematopoietic stem cells to constitute "neural cells" within Applicants interpretation of this term.

Dunbar et al. discloses that hematopoietic stem cells were known in the prior art.

Thus, the claimed compositions are disclosed in the prior art.

Claims 82-86 are rejected under 35 U.S.C. 102(b) as being anticipated by Reynolds et al. (1992).

The claims are directed to neural cells.

Claims 82-86 are product-by-process claims. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. The patentability of a product does not depend on its method of production. See MPEP 2113. Thus, the claims read on neural cells disclosed in the prior art, as discussed below. There are no structural limitations to distinguish the claimed cells from any other neural cell.

Reynolds et al. (1992) disclose neurons, astrocytes, and neuroepithelial stem cells. All three cell types qualify as "neural cells" as instantly claimed.

Thus, the claimed compositions are disclosed in the prior art.

Claims 72-86 are rejected under 35 U.S.C. 102(b) as being anticipated by Azizi et al. (1998).

The claims are directed to neural cells.

Claim 81 is directed to an isolated human multipotent neural progenitor cell obtainable from umbilical cord blood, wherein said neural progenitor cell exhibits both an increase in the expression of genes associated with neurogenesis and a decrease in expression of genes associated with hematopoiesis when said neural progenitor cell is in the presence of an effective amount of a differentiation agent.

Claims 82-86 are product-by-process claims. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. The patentability of a product does not depend on its method of production. See MPEP 2113. Thus, the claims read on neural cells disclosed in the prior art, as discussed below. There are no structural limitations to distinguish the claimed cells from any other neural cell.

Azizi et al. (1998) disclose human marrow stromal cells (MSCs). They also examined the effects of direct injection of human MSCs into the brains of rats and found that the cells migrated from the injection site along known pathways for migration of neural stem cells to successive layers of the brain. Since mesenchymal stem cells are also present in umbilical cord blood the cells disclosed by Azizi et al. meet all the claim limitations.

Thus, the claimed compositions are disclosed in the prior art.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH

shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (703) 306-9155. The examiner can normally be reached Monday through Friday from 10:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The central official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to William Phillips, whose telephone number is (703) 305-3482.

Art Unit 1632 will be moving to the new USPTO headquarters on January 13, 2004. After that date, Examiner Falk can be reached at (571) 272-0728 and Examiner Reynolds can be reached at (571) 272-0734.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER